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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/559,764	04/27/2000	Hans Jakob Flodgaard	5694.200-US	2707

7590 09/06/2002

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EXAMINER
ROARK, JESSICA H

ART UNIT	PAPER NUMBER
1644	16

DATE MAILED: 09/06/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/559,764	Applicant(s) FLODGAARD ET AL.	
	Examiner Jessica H. Roark	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 June 2002 and 29 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-11,15-42 and 53-60* is/are pending in the application.

4a) Of the above claim(s) *7-11 and 15-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *53-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 April 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/20/02 has been entered.

2. Applicant's amendment, filed 6/20/02 (Paper No. 14), is acknowledged.
Claims 43-52 have been cancelled. Claims 1-6 and 12-14 have been cancelled previously.
Claims 53-60 have been added.
Claims 7-11 and 15-42 and 53-60 are pending.

Claims 7-11 and 15-42 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

Claims 53-60 with respect to the elected species of SIRS (systemic inflammatory response syndrome) *are under consideration in the instant application.*

Drawings

3. Formal drawings have been submitted which fail to comply with 37 CFR 1.84.
Please see the form PTO-948 previously provided as part of Paper No. 9.

Applicant's indication in the Response filed 10/16/01 that formal drawings will be filed upon issuance of a notice of allowability is acknowledged. However, drawing corrections are no longer being held in abeyance by the Office. Please note the new requirements for timing of corrections.

A. Correction of Informalities -- 37 CFR 1.85
New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. *The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.*

B. Corrections other than Informalities Noted by Draftsperson on form PTO-948.
All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections
*Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in **ABANDONMENT** of the application.*

4. Applicant is reminded to amend the Brief Description of the Drawings to reflect the numbering used in the Figures and to describe each individual panel.

For example, , "Figure 5 shows" should read -- Figures 5A-5B show --, and "Figure 11 shows" should read -- Figures 11A-11C show --.

Appropriate correction is required.

5. This Office Action will be in response to applicant's arguments, filed 6/20/021 (Paper No. 14). The rejections of record can be found in the previous Office Actions (Paper Nos. 8 and 12).

It is noted that New Grounds of Rejection are set forth herein.

6. Applicant's cancellation of Claims 43-52 have obviated the previous objections and rejections with respect to these claims.

Priority

7. Neither provisional application 60/12,748 (4/29/99) nor 60/157,384 (10/1/99) appears to provide adequate written support for an antibody to an epitope of HBP that interacts with kininogen; thus claims 53-60 are considered to have the priority date of the instant application (4/27/00).

Applicant in the response filed 6/20/02 has pointed to various locations in the provisional documents for support for this limitation.

Applicant argues that results disclosed in Example 2 of each priority document provides a basis for the ordinary artisan to deduce that HBP interacts with kininogen and that therefore methods utilizing an antibody which binds to the epitope of HBP that interacts with kininogen are supported.

However, it is noted that entitlement to a filing date does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed. Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977).

Applicant's arguments are therefore not found convincing in the absence of adequate written support for the instantly claimed limitation of an antibody that binds an epitope of HBP which interacts with kininogen.

Specification

8. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP 608.01(o).

Applicant is requested to identify the written support for claims 53-60, particularly the claimed limitation of *an antibody that binds an epitope of HBP which interacts with kininogen.*

Claim Rejections - 35 USC § 112 second paragraph

9. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 53-60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 53-60 are indefinite in that they only describe the protein bound by the antibody by the arbitrary protein name "heparin binding proteins (HBP)". While the name itself may have some notion of the activity of the protein, there is nothing in the claims which distinctly claims the protein. For example, others in the field may isolate the same protein and give such an entirely different name (e.g., see Rasmussen et al. FEBS Lett. 390:109-112 1996, of record). In addition, other proteins are known in the art that also bind to heparin and therefore constitute "heparin binding proteins", e.g., collagen. Applicant should particularly point out and distinctly claim the HBP by claiming characteristics associated with the protein (e.g. a SEQ ID NO:, etc.). Claiming biochemical molecules by a particular name given to the protein by various workers in the field fails to distinctly claim what that protein is and of what the composition is made.

It is noted that the amendments filed 10/16/01 and 6/20/02 require that the mammal to which the antibody is administered produce an heparin binding protein having a structure related to SEQ ID NO:1 and various functions.

Applicant argues in the response filed 6/20/02 that the combination of structural and functional properties recited in the newly added claims renders the term "heparin binding protein" definite.

However, there is no requirement that the antibody bind the HBP described as produced by the mammal. Thus the instant claims still do not set forth the metes and bounds of the protein bound by the antibody in the instant methods.

It is suggested that any limitations regarding the HBP be written to *clearly modify the HBP bound by the antibody* administered in the method, e.g., by indicating that the HBP bound by the antibody is the same as that produced by the mammal ("wherein said antibody binds to an epitope of *said* HBP").

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

Claim Rejections - 35 USC § 112 first paragraph

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 53-60 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The specification as originally filed does not provide support for the invention as now claimed. *This is a New Matter rejection for the following reasons*:

Applicant's amendment asserts that no New Matter has been added. However, the specification does not appear to provide an adequate written description of "an antibody that binds an epitope of HBP which interacts *with kininogen*".

The specification does disclose an antibody that binds to an epitope of HBP that binds to the *prekallikrein-H-kininogen complex* and activates release of bradykinin and it use in a methods that treating disorders resulting from bradykinin release (e.g., page 7 of the specification at lines 11-19).

However, there does not appear to be adequate support for a method comprising administering an antibody that binds to an epitope of HBP that interacts with *kininogen*. The instant claims now recite limitations which were not clearly disclosed in the specification and claims as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in the present claims, which did not appear in the specification or original claims, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

In Purdue Pharma L.P. v Faulding Inc., 56 USPQ2d 1481, 1486 (CA FC 2000) the Court noted with respect to In re Ruschig 379 F.2d 990, 154 USPQ 118 (CCPA 1967) that "Ruschig makes clear that one cannot disclose a forest in the original application, and then later pick a tree out of the forest and say 'here is my invention.' In order to satisfy the written description requirement, the blaze marks directing the skilled artisan to that tree must be in the originally filed disclosure. See [In re Ruschig] at 994-95, 154 USPQ at 122; Fujikawa, 93 F.3d at 1570-71, 39 USPQ2d at 1905; Martin v. Mayer, 823 F.2d 500, 505, 3 USPQ2d 1333, 1337(Fed. Cir. 1987) ("It is 'not a question of whether one skilled in the art might be able to construct the patentee's device from the teachings of the disclosure. ... Rather, it is a question whether the application necessarily discloses that particular device.'") (quoting Jepson v. Coleman, 314 F.2d 533, 536, 136 USPQ 647, 649-50(CCPA 1963))".

Neither is obviousness the standard for the addition of new limitations to the disclosure as filed. It is noted that entitlement to a filing date does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed. Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977). New Matter is a written description issue.

Applicant is required to cancel the New Matter in the response to this Office Action.
Alternatively, Applicant is invited to clearly point out the written support for the instant limitations.

13. Claims 53-60 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims recite a method comprising administering an antibody that binds to an epitope of HBP which interacts with kininogen.

It is again acknowledged that Applicant's disclosure appears to support a role for HBP in the release of bradykinin from H-kininogen after cleavage by kallikrein (e.g., the Examples on pages 44-48 of the specification). However, the disclosure does not appear to enable the actual binding of an epitope of HBP to kininogen, and therefore does not appear to enable an antibody to the proposed epitope of HBP and its use in the instant methods.

As previously noted, the state of the art clearly recognized a role for HBP in inflammation (e.g. reviewed in Pereira J. Leukocyte Biol. 57:805-812, 1995, of record). For instance, Pereira teaches that the protein CAP37, which as noted supra is the same protein as the HBP of the instant invention, is involved in inflammation by virtue of multiple functions: binding of endotoxin (LPS/lipid A), direct microbicidal activity, and the recruitment of cells to the inflammatory site (see entire document, especially "Discussion" on page 810). Applicant provides additional data supporting a role for HBP in mediation of inflammation, as assessed primarily by monitoring changes in endothelial cell (EC) permeability.

However, although Applicant provides evidence that blocking HBP (by binding to aprotinin) or blocking various steps in the direct activation of bradykinin inhibits the HBP-induced increase in EC permeability; it is unpredictable as to whether HBP and kininogen directly interact (i.e., that an epitope of HBP specifically binds kininogen), or whether intermediaries exist that mediate the observed effect. In the absence of objective evidence or working examples indicating that an epitope on HBP specifically binds kininogen; the skilled artisan would find it highly unpredictable that an antibody having the instantly recited properties could be produced and could be used as an HBP antagonist in the prevention or treatment of any disorder. Before the skilled artisan could successfully produce a monoclonal antibody to the epitope; the skilled artisan would first have to ascertain whether or not an HBP epitope that binds kininogen exists. Without knowledge that the epitope exists, the experimentation left to those skilled in the art to practice the instant method is unnecessarily, and improperly, extensive and undue.

Applicant has indicated in the Remarks filed 6/20/02 that the Declaration of Dr. Renne (filed 8/29/02) provides objective evidence that HBP and kininogen do directly interact and therefore obviates this rejection.

The Renne Declaration under 37 CFR 1.132 filed 8/29/02 has been fully considered but is insufficient to overcome the rejection set forth supra of claims 53-60 under 35 USC 112, first paragraph for lack of enablement.

While the Renne Declaration provides data to support that HBP can *displace* HK assembled on the surface of endothelial cells or on immobilized heparin sulfate, these data do not appear to support a physical interaction between HBP and kininogen (or the prekallikrein-H-kininogen complex). Rather, the fact that HBP can displace HK only supports that HBP and HK can compete for binding to a third molecule. Olofsson et al. (J. Clin. Invest. 1999; 104(7):885-894) teach that HBP binds to endothelial cell surface proteoglycans and review that HBP was known in the art to bind heparin sulfate (see entire document, particularly "Results" on pages 889-890). In each of the experiments described a non-HK substrate is available for binding by HBP. Consequently, the experiments do not address the instant limitation requiring that the antibody administered in the method bind to an epitope of HBP that interacts with kininogen (or the prekallikrein-H-kininogen complex).

The rejection of record is therefore maintained as it applies to the instant claims.

Applicant is again invited to provide objective evidence that the instant claims are enabled with respect to an antibody that binds to an epitope of HBP that interacts with kininogen.

35 U.S.C. §§ 102 and 103

14. While the instant claims reciting a method comprising administering an antibody that binds to an epitope of HBP which interacts with kininogen do not appear to be enabled for the reasons of record and set forth supra, it is noted (as acknowledged previously) that a method of preventing or treating an inflammatory disorder resulting from release of bradykinin and alterations in endothelial cell permeability by administering an antibody that is an HBP antagonist is enabled.

The Office cannot test whether an antibody antagonist of HBP that functions in a method of preventing or treating an inflammatory disorder does so by a mechanism involving inhibition of release of bradykinin and alterations in endothelial cell permeability and is an antibody that binds to an epitope of HBP which interacts with kininogen.

However, if such an epitope exists, then an antibody that binds HBP and functions in a method of preventing or treating an inflammatory disorder resulting from release of bradykinin and alterations in endothelial cell permeability would appear to necessarily bind to the epitope of HBP that interacts with kininogen, since the end result of administering an antibody antagonist of HBP and administering an antibody that binds an epitope of HBP that binds kininogen appears to be the same (inhibition of inflammation).

Therefore, the rejections of record under 35 USC 102(e) and 35 USC 103(a) in view of Oppenhelm et al. (US Pat. No. 5,837,247, of record) have now been extended to address the currently non-enabled claims, in view of the applicability of the rejection should the instant claims eventually be shown to be enabled.

Claim Rejections – 35 U.S.C. §§ 102 and 103

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

16. Claims 53-55 and 60 are rejected under 35 U.S.C. 102(e) of as being anticipated by Oppenhelm et al. (US Pat. No. 5,837,247, of record, see entire document), as evidenced by Rasmussen et al. (FEBS Lett. 390:109-112 1996, of record, see entire document).

Applicant notes in the Remarks filed 6/20/02 that the claims to which this rejection was originally applied have been cancelled, thereby obviating the rejection.

As noted supra in #14, after further review the rejection has been extended to claims which at present do not appear to be enabled in view of the applicability of the teachings of the reference if the instant claims are later shown to be enabled.

Oppenhelm et al. teach a method for reducing or inhibiting an inflammatory disorder in a human subject comprising administering a monoclonal antibody antagonist of CAP37/HBP (see entire document; e.g., column 2, especially lines 57-67 and columns 9-10, especially bridging paragraph).

CAP37 and HBP are the same protein, as evidenced by Rasmussen et al. (e.g., "Introduction"), and would therefore inherently possess the functional and structural properties of HBP recited in instant claim 53.

Administration of what appears to be the same compound (an anti-HBP antibody) would inherently result in decrease in bradykinin release and the downstream effect of attenuation of alterations in endothelial cell permeability in a mammal, since the functional properties of the compound are inherent. Applicant is reminded that when a claim recites using an old composition or structure (e.g. an HBP-specific antibody) and the use is directed to a result or property of that composition or structure (e.g., effective to decrease release of bradykinin), then the claim is anticipated. See MPEP 2112.02. Also, see Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc. 58 USPQ2d 1508 (CA FC 2001); Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

Applicant is further reminded that the courts have held that there is no requirement that those of ordinary skill in the art know of an inherent property, such as the inherent decrease in release of bradykinin in response to administering an antibody to HBP. See MPEP 2131.01(d) and MPEP 2112 - 2113 for case law on inherency

Systemic inflammatory response syndrome encompasses multiple inflammatory disorders; thus claim 60 is anticipated (see MPEP 2131.02).

Finally, no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitation of decreasing release of bradykinin and altering endothelial cell permeability would be an inherent property of a method comprising administering an anti-CAP37/HBP antibody to reduce or inhibit an inflammatory disorder. Further, it appears that any antibody that binds HBP and inhibits inflammation must bind the same epitope of HBP.

Applicant is invited to provide objective evidence that the antibodies taught by Oppenhelm et al. do not inherently possess the instantly recited properties.

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

18. Claims 56-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oppenhelm et al. (US Pat. No. 5,837,247, of record) as evidenced by Rasmussen et al. (FEBS Lett. 390:109-112 1996, of record); in view of Grunfield et al. (US Pat No. 5,660,826, of record).

Applicant notes in the Remarks filed 6/20/02 that the claims to which this rejection was originally applied have been cancelled, thereby obviating the rejection.

As noted supra in #14, after further review the rejection has been extended to claims which at present do not appear to be enabled in view of the applicability of the teachings of the reference if the instant claims are later shown to be enabled.

The claims are drawn to methods comprising administering specific dosages of an HBP/CAP37 antagonist wherein the antagonist is an antibody.

Oppenhelm et al. as evidenced by Rasmussen et al. have been discussed supra.

Oppenhelm et al. as evidenced by Rasmussen et al. teach a method of inhibiting inflammation by administering an antagonist anti-HBP antibody.

Oppenhelm et al. do not explicitly teach the dosage of administration of the antibody antagonist of HBP.

Grunfield et al. teach and claim a method comprising administering to a patient suffering from risk of systemic inflammatory response syndrome an effective amount of an antibody inhibitor wherein the antibody inhibitor is administered in the pharmaceutically effective amount of 1μg/kg to 10mg/kg (see entire document, especially claims 1 and 2). Grunfield et al. also teach that the dose is subject to a great deal of therapeutic discretion, and that higher doses may be needed (e.g., column 4, especially lines 23-37).

Given the teachings of Grunfield et al. with respect to dosages of administering antibodies for treating systemic inflammatory response syndrome conditions such as shock; it would have been obvious to the ordinary artisan at the time the invention was made to utilize similar dosages of antibodies to HBP, especially since the therapeutic use of anti-HBP antibodies taught by Oppenhelm et al. is for inhibiting inflammation. The ordinary artisan would have been motivated to utilize these similar dosages in light of the similarities of the therapeutic modality and the conditions treated. In addition, given these similarities, the ordinary artisan would have had a reasonable expectation that the effective dose of the antibody antagonist of HBP was similar to or encompassed by the range taught by Grunfield et al. Finally, the ordinary artisan would have been motivated to formulate the antibody composition in an amount of from about 10 mg to 1g per unit dosage in order to provide sufficient quantities of the antibody preparation in a reasonably compact dosing.

While many of the claim limitations are intrinsic to the method taught by Oppenhelm et al., the motivation to formulate the antibody at the recited concentration and administer it at the recited dosages is not affected by these intrinsic properties. Instead, the ordinary artisan would have been motivated based simply upon the need to formulate what appears to be the same product at a concentration and dosage appropriate to treat the disorder. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

19. No claim allowed

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica H. Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday, 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Jessica Roark, Ph.D.
Patent Examiner
Technology Center 1600
September 5, 2002

Phillip Gambel
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9/5/02